THE EFFECT OF HOMEOPATHICALLY PREPARED *ARNICA MONTANA 6C* ON BLEEDING, PROTHROMBIN AND ACTIVATED PARTIAL THROMBOPLASTIN TIMES *IN VIVO*

A mini dissertation submitted to the Faculty of Health Sciences, University of Johannesburg, Johannesburg, in partial fulfillment for the degree of Master of Technology : Homeopathy

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DECLARATION

I declare that this mini dissertation is my own, unaided work. It is being submitted for the degree of Masters of Technology : Homeopathy at the University of Johannesburg, Johannesburg. It has not been submitted before for any degree or examination in any other University.

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ABSTRACT

Haemostasis is an internal mechanism to stop bleeding from a damaged blood vessel. Conceptually this process occurs in a number of essential steps following tissue injury. Although the herbal preparation of *Arnica montana* has been well documented for its tendency to prolong bleeding, according to the Law of Similars, homeopathically prepared *Arnica montana* 6C is well indicated for traumatic injuries and post surgical bruising. *Arnica montana* 6C can be used when there is mechanical trauma that causes wounds, haemorrhages, haematomas, sore-bruised bone and muscular pains, inflammations, fractures, muscular strains and sprains. The remedy is often prescribed before and immediately after surgery to reduce post-operative pain and to speed up recuperation.

Three *in vitro* studies conducted at the Technikon Witwatersrand (now the University of Johannesburg) on various potencies of homeopathically prepared *Arnica montana* showed lowered overall coagubility of blood, but no significant difference between the experimental and control groups. Bengsch (2000), Hohl (2005), Vermeulen (2000) and van Tonder (2005) recommended that studies on the effect of homeopathically prepared *Arnica montana* on blood coagulability be repeated *in vivo*.

This study formed part of a three part *in vivo* study to determine the effect of *Arnica montana* homeopathic preparations on blood coagulation by measuring the Bleeding Time (BT), activated Partial Thromboplastin Time (aPTT) and Prothrombin Time (PT). This study investigated the effect of *Arnica montana* 6C on these measurements.

Eighty participants were allocated a participant number and randomised by the research supervisor into four groups of twenty participants. Twenty participants were in the placebo group that was shared by all three studies. Twenty participants were allocated to the experimental group for this study. The study was conducted over a period of two weeks at the University of Johannesburg (UJ) Doornfontein Campus Homeopathy Health Centre. Consenting participants were screened by means of a questionnaire (Appendix D) regarding relevant medical history and other background information. A case history was taken and a physical examination was performed. Any prospective participants that were diagnosed with and/or suffer from hypertension, hypotension, heart disease, a

bleeding disorder, anaemia, iron or any vitamin deficiency, liver disease, malaria or are currently on aspirin or anticoagulants (Appendix D) were excluded from the study.

The bleeding time was measured by a trained medical technologist using a standardised bleeding time technique. Blood samples drawn by a phlebotomist went for coagulation tests comprising of aPTT and PT at the NHLS Main Haematology laboratory of the Johannesburg Hospital. Twenty participants were given a 25mL bottle of *Arnica montana* 6C in 20% ethanol. Twenty participants received an identical bottle containing only 20% ethanol. All participants were requested to take ten drops twice a day for two weeks. All three coagulation test measurements were performed again at the end of the second week.

The BT, PT and aPTT results were analysed by using ordinary descriptive statistics such as mean and standard deviation. Changes over time in blood coagulation were ascertained utilising ANOVA (analysis of variance). The results showed that there is no statistically significant difference between the experimental and control group in BT, aPTT and PT. There was also no statistically significant difference between the first BT, PT and aPTT before medication and the second BT, PT and aPTT after two weeks of medication.

The results of the study support the hypothesis that *Arnica montana* 6C would have no effect on the bleeding or coagulation times *in vivo*. These results support the view that prescribing the remedy before surgery is not likely to increase the post surgical risk of haemorrhage.

DEDICATION

This research report is dedicated to my friends, family and also in loving memory of my father Dr. B.F.M. Nkunjana (1947 – 1998). Thanks for your love, support, encouragement and patience.

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LIST OF ABREVIATIONS

ANOVA – Analysis of Variants

aPTT – activated Partial Thromboplastin Time

BT – Bleeding Time

C – Centesimal

D - Decimal

INR – International Normalised Ratio

ISI – International Sensitivity Index

NHLS – National Health Laboratory Services

PT – Prothrombin Time

Sig. – p-value

UJ – University of Johannesburg

X - Decimal

CHAPTER 1

INTRODUCTION

1.1 Problem statement

The herbal preparation of *Arnica montana* has been well documented for its tendency to prolong bleeding (Schroder *et al.*, 1990). According to the fundamental principle of Homeopathy: "Let likes be cured by likes" homeopathically prepared *Arnica montana* 6C is well indicated for traumatic injuries and post surgical bruising (Tyler, 1992). *Arnica montana* 6C is used when there is mechanical trauma that causes wounds, haemorrhages, haematomas, sore-bruised bone and muscular pains, inflammations, fractures, muscular strains and sprains. It has an anti-platelet effect and is used in heart and circulation problems. *Arnica montana* is also used in lower potencies but not in mother tincture, locally on the skin for dermatitis, boils, superficial phlebitis and insect bites. It is also used as a mouthwash for inflamed gums and mouth ulcers (Vermeulen, 1997). *Arnica montana* 6C is also taken internally before and immediately after surgery to reduce post-operative pain and to speed up recuperation (Scott and Barlow, 2003).

Similar *in vitro* studies conducted at the Technikon Witwatersrand (now the University of Johannesburg) on various homeopathic potencies of *Arnica montana* showed lowered overall coagubility of blood, but no significant difference between the experimental and control groups. Bengsch (2000), Hohl (2005), Vermeulen (2000) and van Tonder (2005) recommended that studies on the effect of homeopathically prepared *Arnica montana* on blood coagulability be repeated *in vivo*.

1.2 Aim of the study

The aim of this study was to investigate the *in vivo* effect of *Arnica montana* 6C on coagulation and bleeding time. This study formed part of a three part *in vivo* study to determine the effect of *Arnica montana* homeopathic preparations on blood coagulation by measuring the Bleeding Time (BT), activated Partial Thromboplastin Time (aPTT) and Prothrombin Time (PT). This study aimed to investigate the effect of *Arnica montana* 6C on these measurements.

1.3 Importance of the study

If the results of this study support the hypothesis that *Arnica montana* 6C will have no effect on the coagulation times *in vivo* it may provide valuable evidence that prescribing the remedy before surgery does not increase the post surgical risk of haemorrhage.

1.4 Hypothesis

The hypothesis of this study is that *Arnica montana* 6C will not have an effect on Bleeding, Prothrombin and activate Partial Thromboplastin Times *in vivo*.

1.5 Null hypothesis

The null hypothesis of this study is that *Arnica montana* 6C will have an effect on Bleeding, Prothrombin and activate Partial Thromboplastin Times *in vivo*.

CHAPTER 2

LITERATURE REVIEW

2.1 Blood and its components

Blood is a fluid that circulates in between the tissues of every organ of the body. It is partly made up of a fluid called plasma. Plasma is mainly composed of water (92%), proteins (7%) and 1% of dissolved organic molecules, ions, trace elements, vitamins, dissolved oxygen and carbon dioxide. The dissolved organic molecules are amino acids, glucose, lipids, and nitrogenous wastes. The ions include sodium, potassium, chloride, hydrogen, calcium and bicarbonate ions (Silverthorn, 2001).

There are also cellular elements that are suspended in the blood. The cellular elements are red blood cells, white blood cells and platelets. The red blood cells are mainly responsible for the gaseous exchange; the white blood cells provide defence against parasites, viruses and bacteria; and the platelets are responsible for blood coagulation. Other functions of blood are transporting nutrients, waste products and hormones (Pockock and Richards, 2004). Blood is also responsible for stabilising the body temperature, regulation of the pH and electrolyte composition of the interstitial fluids (Martini, 2006)

2.2 Blood vessels

The circulatory system can be divided into macrocirculation and microcirculation. The macrocirculation consists of large arteries and veins. Their function is to relay blood form the heart to the tissues and back to the heart. The microcirculation consists of small arterioles, venules and capillaries, which connect the arterioles to the venules. It is responsible for the exchange of gases, electrolytes, food substances and waste products with the surrounding tissue cells (Haen, 1995).

The blood vessel wall is made up of three layers: tunica intima, tunica media and tunica adventitia. The tunica adventitia is the outermost layer and it forms a connective tissue sheath that covers the outside of the blood vessel. In arteries this layer consists of collagen and elastic fibres. In veins it is thicker than the tunica media and it consist of collagen, elastic and smooth muscle fibres (Martini, 2006).

The tunica media is the middle and in arteries the thickest of the three layers. It contains concentric sheets of smooth muscle tissue. These cells contract to decrease and relax to increase the lumen of the blood vessel. This helps to accommodate the increase and the decrease in the blood flow (Martini, 2006).

The tunica intima is the innermost layer of the blood vessels. It consists of an endothelial cell lining and subendothelial connective tissue. The tunica intima is separated from the tunica media by the elastic lamina interna. The structure and function of the endothelial cells differ according to the location of the blood vessel that they are lining. In the resting state of these cells, their structure and function is the same. Their function is to promote the maintenance of the blood vessel in its fluid state, they assist in supplying nutrients to the subendothelial structures and they act as a barrier to macromolecules and particulate matter circulating in the bloodstream (Dacie and Lewis, 2002). The tunica intima manufactures the substances necessary for haemostasis (Table 1) (Hudson and Bunting, 1994).

Table 1: Substances secreted by endothelial cells and their functions (Hudson and Bunting, 1994).

Substance	**Function**
ADPase	Degrades ADP (adenosine diphosphate).
Collagen	Activates coagulation factors and stimulates platelets adhesion.
Glycocalyx	Coats the endothelial surface with heparin sulphate.
Prostacyclin	Dilates vessels and inhibits platelets aggregation.
Thrombomodulin	Neutralises thrombin and enhances protein C activity.
Tissue Plasminogen Activator (tPA)	Assists in clot breakdown.
Von Willebrand's factor	Regulates platelet adhesion.

2.3 Platelets

Platelets are small, bluish, discoid granular structures that are two to three micrometers in diameter. Their normal concentration in the blood is between 150.000 and 400.000 per microlitre. Platelets are derived from large lymphoid cells in the bone marrow called megakaryocytes (Haen, 1995). A platelet has a lifespan in the blood of about eight to twelve days after which it is eliminated from the circulation by the macrophages. More than a half of these platelets are removed by the macrophages in the spleen when they pass through the spleen trabeculae (Guyton and Hall, 2000). Platelets have openings on their surface called canaliculi. These openings increase the surface area of the platelets to adsorb the coagulation factors necessary for the clotting process (Haen, 1995). Platelets function like normal cells, even though they do not have nuclei and cannot reproduce. In their cytoplasm they have actin and myosin that are similar to the ones found in muscle cells. They have golgi apparatus and endoplasmic reticulum that are responsible for synthesis of enzymes and storage of calcium ions. They also have mitochondria and enzyme systems that form adenosine diphosphate and adenosine triphosphate (Guyton and Hall, 2000).

Platelets function by initiating and controlling the clotting process by releasing enzymes and other clotting factors. They clump together at the injury site to form a platelet plug that slows the loss of blood while clotting occurs. Then, the contraction of platelet filaments shrinks the clot and reduces the size of the break in the vessel wall (Martini, 2006). Platelets are responsible for closing the minute ruptures in very small blood vessels. This is called the platelet-plugging mechanism and it occurs hundreds of times daily. A person who has a decreased amount of platelets develops hundreds of small haemorrhagic areas under the skin and in the internal organs (Guyton and Hall, 2000).

2.4 Haemostasis

Haemostasis in its simplest form means "blood" (*haima*) and "stop" (*stasis*). It is a process of preventing blood loss following blood vessel damage by forming a blood clot (Martini, 2006). This process helps to close the broken blood vessel, stop loss of blood and is also a step to healing (Hillman, 1998). The pro-coagulant proteins gather on the platelet surface and promote blood clot formation. The anti-coagulant proteins prevent uncontrolled extension of this clot and allow clot breakdown once vessel healing has been initiated (Kisuck *et al.*, 2006). Haemostasis is divided into

the vascular phase, the platelet phase, the coagulation phase, the conversion of fibrinogen into fibrin and the conversion of prothrombin into thrombin (Martini, 2006).

2.4.1 The vascular phase

Injury to the blood vessel triggers the contraction and spasm of the blood vessel wall, which decreases the diameter of the vessel at the site of the injury. This blood vessel response aims to limit the extent of blood loss at the site of injury. Endothelial cells in the blood vessel contract to expose the basement membrane to which platelets adhere (Renne *et al.*, 2005). The endothelial cells also release chemical factors and hormones, which include adenosine diphosphate, tissue factor, prostacyclin and endothelins (peptide hormone), which further promote contraction and spasm of the blood vessel wall (Martini, 2006).

2.4.2 The platelet phase

The circulating blood platelets are activated when they come into contact with the basement membrane and they change their shape by forming pseudopods. Activated platelets adhere to the endothelial surfaces, basement membrane and the exposed collagen fibres. They then aggregate and undergo degranulation and release a number of substances including adenosine diphosphate (ADP), calcium ions, serotonin, platelet factor IV and β-thromboglobulin, generation of thromboxane A2 and thrombin. The ADP, calcium ions, thrombin and thromboxane A2 provide a strong stimulus for further platelet activation and aggregation. The thrombin stimulates fibrinogen conversion to fibrin to stabilise the aggregate as a fibrin clot, which will be explained later. The result of this is further activation of platelets (Hillman, 1998).

2.4.3 The coagulation phase

The balance between the procoagulants and the anticoagulants determines whether or not the blood will coagulate. Normally the anticoagulants predominate and the blood does not coagulate. If a blood vessel is ruptured, procoagulants dominate and the surface of the activated platelets allows for coagulation factor interaction. The net effect is the formation of the blood clot at the injury site (Guyton and Hall, 2000).

These reactions are initiated by activation of clotting factors. Activation of factor VII or factor XI (Table 2) is required for the beginning of these coagulation pathways (Figure 1). When blood vessels and surrounding tissues are damaged, these two factors are converted from an inactive to an active form, which then creates a clotting cascade. Clotting factor interaction is not haphazard but occurs in a predictable sequential fashion. For simplicity, the sequential clotting factor interaction can be divided into three stages or pathways. These pathways are intrinsic, extrinsic and common pathway (Barbior and Stossel, 1994).

The intrinsic pathway is activated by the contact of factor XII with collagen fibres in the damaged vessel wall and other negatively charged components of the subendothelium. Factor XII is converted into Factor XIIa when it comes into contact with collagen or a foreign surface. Factor XIIa activates factor XI which in turn (factor XIa) activates factor IX to factor IXa. Together with platelets, factor VIIIa (activated form of factor VIII) and calcium, factor IXa activates factor X (Figure 1)(King, 2006).

In the extrinsic pathway alterations of the endothelial cell membrane expose a tissue factor which activates or complexes with factor VII. The factor VIIa-tissue factor complex activates factor X to Factor Xa which activates prothrombin in the common pathway (Hasenstab *et al.*, 2000). Both extrinsic and intrinsic pathways end up in the common pathway. Factor Xa and cofactor Va convert prothrombin into thrombin in the presence of phospholipids and calcium ions (Figure 1) (Howard and Hamilton, 1999).

2.4.4 Conversion of prothrombin into thrombin

Prothrombin (factor II) (Table 2) is a plasma protein that is continually formed by the liver and is constantly used by the body for blood clotting. Vitamin K is required for the formation of prothrombin and the other three clotting factors. Therefore, the lack of vitamin K or liver disease, that prevents the formation of prothrombin, can decrease prothrombin levels which will result in a tendency to bleed. After the prothrombin activator has been formed as a result of rupture of blood vessels or damage to special activator substances in the blood, it activates the conversion of prothrombin to thrombin. Thrombin then activates the conversion of fibrinogen molecules into fibrin threads (Figure 1) (Guyton and Hall, 2000).

Table 2: Blood coagulation factors (Martini, 2006)

	Name	Source	Pathway
I	Fibrinogen	Liver	Common
II	Prothrombin	Liver, requires vitamin A	Common
III	Thromboplastin (Tissue factor)	Damaged tissue, activated platelets	Extrinsic and intrinsic
IV	Calcium ions	Bones, intestines, platelets	Entire process
V	Proaccelerin	Liver, platelets	Extrinsic and intrinsic
VI	No longer used		
VII	Proconvertin	Liver, requires vitamin A	Extrinsic
VIII	Antihaemophilic factor (AHF)	Platelets, endothelial cells	Intrinsic
IX	Christmas factor	Liver, requires vitamin A	Intrinsic
X	Stuart-Prower factor	Liver, requires vitamin A	Extrinsic and intrinsic
XI	Plasma thromboplastin antecedent (PTA)	Liver	Intrinsic
XII	Hageman factor	Liver	Intrinsic; also activates plasmin
XIII	Fibrin-stabilising factor (FSF)	Liver, platelets	Stabilises fibrin, slows fibrinolysis

2.4.5 Conversion of fibrinogen into fibrin

Fibrinogen is a high molecular weight protein that is formed in the liver. Liver disease affects the circulating fibrinogen negatively by decreasing its concentration and that of prothrombin and this leads to poor coagulation, if coagulation will occur at all. Blood coagulates when fibrinogen is converted to fibrin. Fibrin changes spontaneously to form a meshwork that is called a clot. Activated thrombin is the enzyme that is responsible for this conversion (Tuddenham *et al*, 1994).

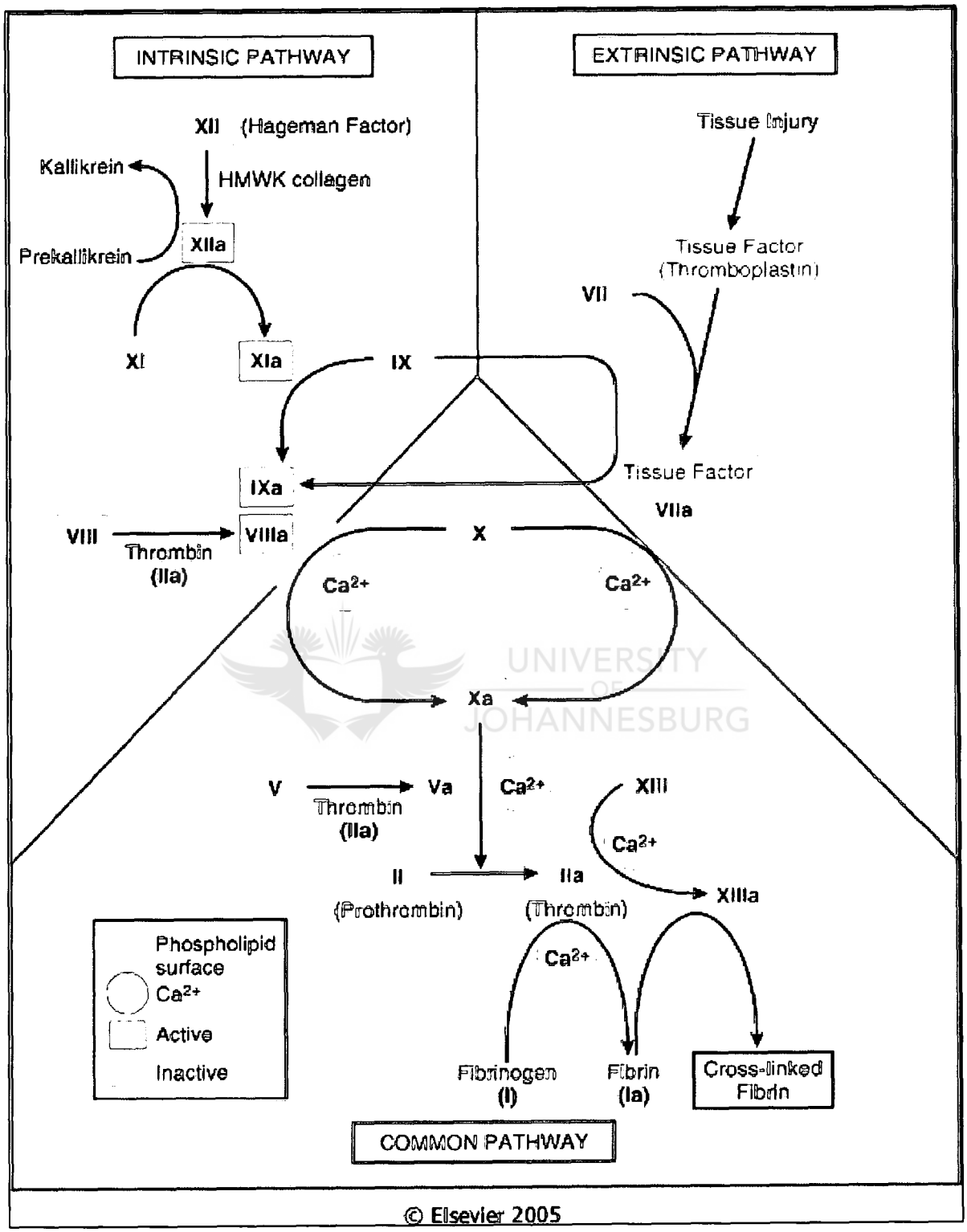

Figure 1. Blood coagulation *Downloaded from: StudentConsult (on 10 January 2008 12:18 PM)*

2.5 Blood coagulation screening tests

2.5.1 Bleeding Time

The Bleeding Time is a measurement of how long it takes to stop bleeding when a fresh cut of defined size is made on the skin. A prolonged Bleeding Time usually indicates a platelet disorder, von Willebrand disease or an abnormality of the blood vessel wall (Koepke, 1991).

2.5.2 The Activated Partial Thromboplastin Time (aPTT)

aPTT is a screening test used to measure the intrinsic pathway of coagulation. The formation of fibrin occurs at a normal rate only if the factors involved in the intrinsic pathway (factors XII, XI, IX and VIII) and the common pathway (factors I, II, V, X and XIII) are present in normal concentrations. Optimal activation is achieved by the addition of a platelet phospholipid substitute, which eliminates the test's sensitivity to platelet number and function, as well as the addition of activators such as kaolin, celite and ellagic acid, which eliminates the variability of activation by glass contact (NHLS Department of Haematology, 1997).

2.5.3 The Prothrombin Time (PT)

PT is the time required to form a fibrin clot when plasma is added to a thromboplastin - calcium mixture. The test is a measure of the extrinsic and common pathway of coagulation involving factors II, V, VII, X as well as fibrinogen. Tissue thromboplastin activates factor VII, which proceeds through the cascade, ultimately generating thrombin. The thrombin thus formed converts fibrinogen to fibrin. The rate of fibrin formation therefore depends on the level of the factors II, V, VII and X and fibrinogen, and thus measures the overall activity of these factors. The results are expressed in International Normalised Ratio (INR). The INR is the ratio of a patient's Prothrombin Time to a normal (control) sample, raised to the power of the International Sensitivity Index (ISI) value for the control sample used (NHLS Department of Haematology, 1997).

2.6 Laws and principles of homeopathy

Homeopathy is as old as medicine itself. Hippocrates (460 – 350 B.C.), who is considered the father of medicine, recognised the Law of Similars as the fundamental principle of medicine. He emphasised that through similar things a disease is produced and through the application of the like, it is cured. Aristotle (384 – 322 B.C.), Galen (130 – 200 B.C.), Theophrasters Bombasters von Hohenheim (1493 – 1541), Dr George Stahl and William Harvey (1578 – 1657) are other historical physicians who also recognised the Law of Similars as the fundamental principle of medicine. This law was rejected by the allopathic medicine because it lacked scientific evidence and was not subjected to systematic, scientific study or used in practice for about two thousand years (Cook, 1989).

Homeopathy is a medical system that was founded by Dr Christian Friedrich Samuel Hahnemann (1755 – 1843). Hahnemann had a broad knowledge of eight languages and translated books to support himself in his student days. He studied and practiced medicine. Hahnemann became disappointed with the principles and methods of medicine of his time early in his career. He decided to stop practicing medicine and he went back to translating books. He was requested to translate Cullen's Materia Medica into German and during this time came across the treatment of fever by using *Cinchona* Bark (quinine). This application of *Cinchona* Bark puzzled Hahnemann who decided to investigate the action of the substance on himself (Blackie, 1990).

2.6.1 Law of Similars

Homeopathy is based on the natural Law of Similars termed "*similia similibus curentur*". This means that a drug causes symptoms when it is administered to a healthy person and it cures the same symptoms when it is administered in a sick person presenting with similar symptoms (Mathur, 2003).

Hahnemann took the *Cinchona* bark himself and he was shocked to find that he developed all the symptoms of a cold. He also noticed that these symptoms disappeared when he stopped taking the *Cinchona*. He discovered that a remedy that was effective in curing a certain disease could produce the symptoms of the same disease when it is given to a healthy person. This meant that the effects of drugs on healthy persons could reveal their specific properties (drug picture) and can be used in

cases where a patient's symptoms matched a specific drug picture. Hahnemann decided to investigate his discovery further on himself and others conducted experiments by using other substances (Boyd, 1989).

2.6.2 Provings in homeopathy

Hahnemann began to investigate a large number of other substances. He did this by administering substances and known remedies to healthy individuals. The symptoms that were produced in these healthy individuals were recorded and compiled systematically. He called this a "proving". The strengths of the symptoms were rated numerically. The symptoms of different remedies were gathered from different provings and they were recorded in a Materia Medica (Vithoulkas, 1990). The Materia Medica represents a large collection of accurate observations, where an indicated remedy is selected, based on its symptom picture similarity to that of the diseased individual. The remedy that most closely matches the presenting symptoms is called the "*similimum*" (Blackie, 1990).

2.6.3 Potentisation

Hahnemann noticed that after a small but material dose of an indicated remedy was given in the crude form there was aggravation of symptoms before there was an improvement. He discovered that when a remedy was diluted and succussed (shaken vigorously) the improvement of symptoms usually started without an aggravation. He called this potentisation and he used this method to manufacture his remedies (Boyd, 1989).

Potentisation is a process incorporated into homeopathic medicinal manufacturing that employs kinetic energy in order to increase and/or activate the innate medicinal power of substances. Both dilution and succussion are important in producing a clinically effective potency. For each potency level, a standard number of succussions are performed, as well as dilution according to the particular scale being used (Vithoulkas, 1990).

2.6.4 Homeopathic pharmacy

Homeopathic medicines are made from minerals, metals, plants, animal and diseased (and healthy) human products (Chappell, 1994). They are manufactured utilising a method of serial dilution. This enables substances that might otherwise be toxic to be of benefit in effecting a cure in homeopathic treatment. The decimal system utilises a one in ten dilution, with the letter "X" symbolising "10". For example, a 3X potency will designate one part active substance in 10^3 parts inactive solvent. The centesimal scale is a one in a hundred parts substance to solvent, with "C" designating the use of this scale. For example, 6C will represent one part active substance in 100^6 parts inactive solvent (Goel, 2002).

All homeopathic medicines are manufactured according to standardised, recognised Pharmacopoeias. Mother tinctures (crude substances or solutions that are before the first homeopathic dilution) from a variety of sources are macerated in various dilutions of alcohol or glycerine. Mother solutions are manufactured from water-soluble substances. Other crude sources are triturated before further potentisation (Vithoulkas, 1990).

2.6.5 The Single Dose

In homeopathy it is suggested that a remedy does not cure the patient and it is not designed to do so. Fundamentally a person alone has the ability to maintain health and to return to health when sick. Therefore homeopathic remedies act by stimulating the body into natural cure and hence a single minimum dose of an indicated remedy is needed to bring about cure (Vithoulkas, 1990). If there is an improvement after a single dose has been administered there is no need for another dose. A further dose can only be given if the improvement of the condition that is being treated has ceased (Boyd, 1989).

2.6.6 The Single Remedy

Classical homeopathy treats the patient by administering only one remedy at a time. A second remedy can be given only if the symptoms change. This is done as there is no way of knowing which remedy is working or causing adverse effects in a case where two or more remedies are used at the same time. Another reason is that remedy provings provide the drug picture for only a single

substance. The drug pictures of combined substances, or complex homeopathic medicines, are largely unknown (Vithoulkas, 1990).

2.6.7 Individualisation in homeopathy

The single remedy or *simillimum* is chosen by using a wide spectrum of information gathered from the patient and a broad knowledge of homeopathic principles and Materia Medica. The symptoms that are peculiar and characteristic of the patient are valuable. Those that are common to the disease are of least importance. This means that homeopathy treats the person not the disease. Therefore, the *simillimum* is not prescribed on the basis of the diagnosis of the disease but on the way that the individual is reacting to the disease. The symptoms that are gathered from the patient include the mental, emotional and physical characteristic symptoms (Vithoulkas, 1990).

2.7 *Arnica montana*

Arnica montana belongs to the *Asteraceae (Compositae)* family (Sandberg and Corrigan, 2001). It is commonly known as Leopard's Bane, Mountain Tobacco and Fall Herb. It is also known as *Arnica* Flowers, Mountain Daisy, Sneezewort and Wolfsbane. It is mostly found in the mountainous regions of Western North America and Europe. Europeans and Native Americans used the herb for sprains, bruises and wounds (Blumenthal *et al.*, 2000). A North American indigenous tribe used to make a tea from the herb to treat backaches. In Russia it has been used for uterine haemorrhages, myocarditis, arteriosclerosis, angina pectoris and cardiac insufficiency. If the flower heads are crushed and sniffed they may cause sneezing hence its name Sneezewort. In Siberia and central Europe this herb was smoked as a substitute of tobacco and this is how it got the name Mountain Tobacco (Hanrahan, 2001). Physicians who practiced natural medicine of the late nineteenth and early twentieth century recommended the herb for contusions, bruised muscles, mastalgia, cardiac weakness and chronic sores (Blumenthal *et al.*, 2000).

Arnica montana is a fragrant, bitter, and astringent herb that stimulates the immune system and heart, relieves pain and inflammation, and clears fungal and bacterial infections. It is an aromatic, rhizomatous perennial plant with basal hairy leaves that have golden yellow daisy-like flowers (Gibson, 1994). *Arnica montana* has tall stems, that grow from hairy cylindrical rhizomes. The stems usually have one to three flower heads. In the first year most of the leaves grow lower, in a

flat and basal rosette. In the second year the stems become round and hairy. In the stems are sessile leaves that grow in one to three opposite pairs. The central stem may form three or more branches with terminal flower heads. The flower heads are yellow and they have ten to fourteen bright yellow rays. Each ray has three notches at the end and the rays are irregular bent backwards. The flowers appear from June to August. The flowering heads are normally used, while the rhizomes are very rarely used (Hanrahan, 2001).

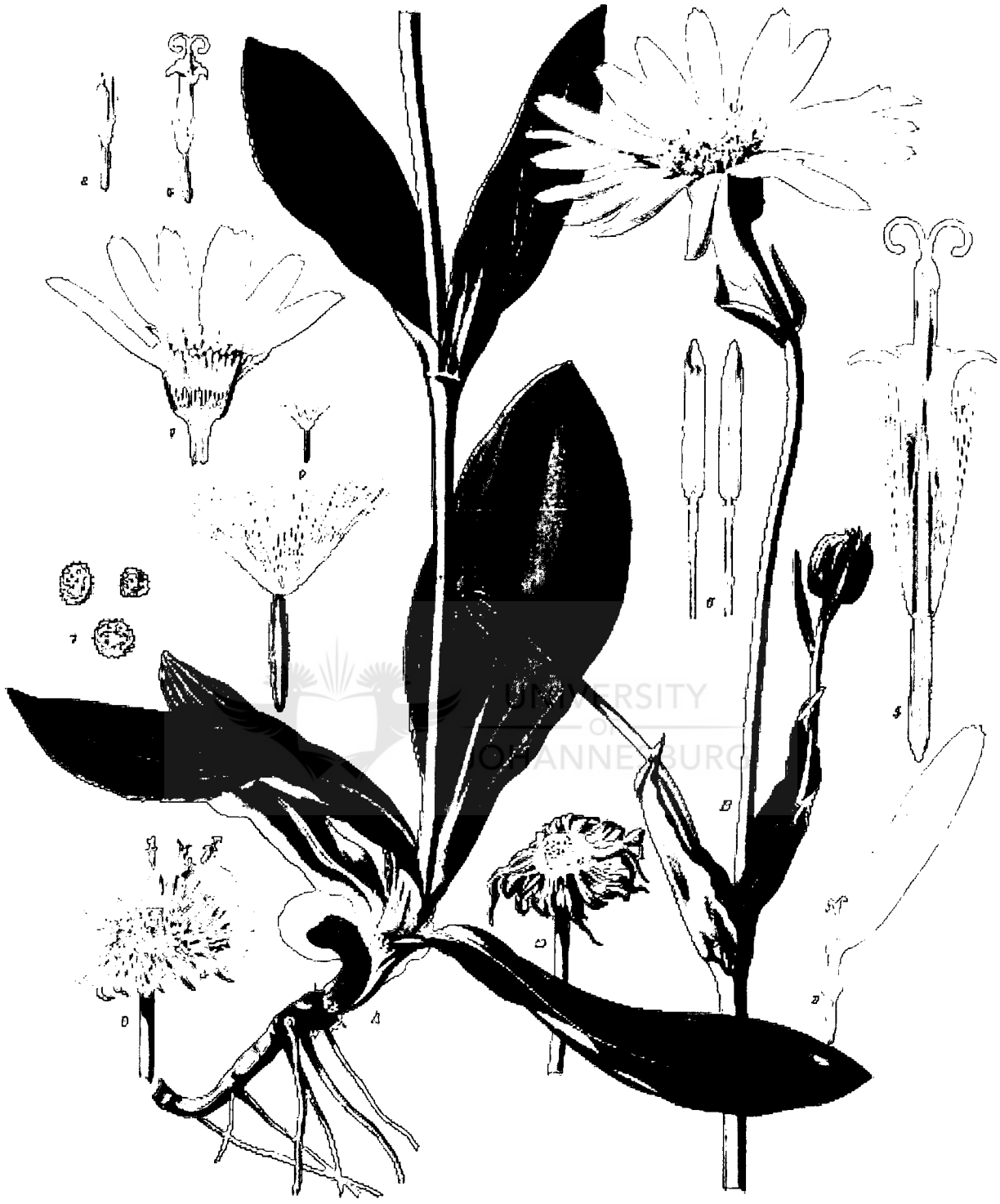

Figure 2. ***Arnica montana*** (Hughes, 2002)

2.7.1 Chemistry and Pharmacology

Arnica montana contains sesquiterpene lactones (helenalin type), flavones, flavonols, volatile oils with thymol, thymolmethylrther and azulene (Van Wyk and Wink, 2004). It also has phenol carbonic acid and coumarins. Helenalin has an antiseptic, analgesic and anti-inflammatory effect (Blumenthal *et al.*, 2000). *Arnica montana* has been used to improve blood flow. It stimulates white blood cells which are responsible for digestion of the congested blood and for dispersing trapped, disorganized fluids from bumped and bruised tissue, joints and muscles (Morrison, 1993).

Coumarins act by inhibiting vitamin K-dependent g-carboxylation of glutamic acid residues in coagulation factors II, VII, IX, and X, and the anticoagulant proteins C and S. Coumarins inhibit the reductases that are required to recycle vitamin K, thus depleting reduced vitamin K that is needed for g-carboxylation. This results in coagulation factors with impaired activity because they are unable to bind calcium and undergo necessary conformation changes (Lichman *et al.*, 2001).

2.7.2 Toxicological picture

Ingestion of large amounts of herbal *Arnica montana* may cause gastroenteritis, dyspnoea, a tendency to haemorrhage (Tyler, 1992), pulse abnormalities, muscular weakness, cardiovascular collapse and death (Spoerke, 1990). It can also cause liver failure, nervous disorders, nausea, vomiting, organ damage, coma and possibly death in children who ingest *Arnica* roots or flowers (Fetrow and Avila, 2000). The application of the mother tincture on the skin may cause dermatitis. Long-term use on the skin may cause eczema, vesicles or even necrosis (Blumenthal *et al.*, 2000). The mother tincture can cause abortion if it is taken internally during pregnancy (Van Wyk and Wink, 2004).

2.7.3 Homeopathic uses of *Arnica montana*

The homeopathically prepared *Arnica montana* (ie. potentised preparation of the herb) is used when there is mechanical trauma that causes wounds, haemorrhages, haematomas, sore-bruised bone and muscular pains, inflammations, fractures, muscular strains and sprains. It is used locally on the skin for dermatitis, boils, superficial phlebitis and insect bites. It is also used as a mouthwash for inflamed gums and mouth ulcers (thrush). It has been noted to have an anti-platelet effect and is

used in heart and circulation problems (Vermeulen, 1997). It is also taken internally (in a homeopathic potency) before and immediately after surgery to reduce post-operative pain and to speed up recuperation (Scott and Barlow, 2003). Tyler (1992) also names *Arnica montana* as the remedy indicated for severe contusions, lacerations, blunt injuries, post tooth extraction and other surgical operations.

Table 3. Materia Medica clinical applications and characteristic symptoms of *Arnica montana*

Area of Action	**Indications**
Mind	Fear of touch, of sickness, of instant death, of cardiac distress at night, of space, of public places (Tyler, 1992; Vermeulen, 1997); delirium tremens, muttering delirium (Tyler, 1992), vertigo, ailments from typhoid and malarial fevers, after mental strain or shock; unconscious, when spoken to answers correctly, but relapses; says there is nothing the matter with him. Wants to be let alone (Tyler, 1992; Vermeulen, 1997).
Head and nervous system	Headaches, meningitis from trauma, alopecia, confusion, apoplexy, brain haemorrhage (Vithoulkas, 1995), chorea and paralysis, hot head with cold body; confused; brain hyperaesthesia, with sharp, pinching pains. Scalp feels contracted, cold spot on forehead. Chronic vertigo; motion sickness (Tyler, 1992; Vermeulen, 1997).
Eyes	Diplopia from trauma, retinal haemorrhages, muscular paralysis, photophobia and exophthalmos, bruised, sore feeling in eyes after close work, feel tired and weary after sight-seeing and looking at moving pictures (Vermeulen, 1997).
Ears	Tinnitus caused by head congestion (Vermeulen, 1997), dull hearing after concussion and bleeding (Tyler, 1992).
Nose	Epistaxis after trauma, after washing the face and during typhoid fever; rhinitis, post nasal drip and empyema of maxillary sinus, haemorrhage after every fit of coughing of dark fluid blood (Vermeulen, 1997; Vithoulkas, 1995).
Face	Paralysis of face, burning and redness of face (Vermeulen, 1997; Vithoulkas, 1995), painful acne, puffed cheeks, herpes in face (Vermeulen, 1997).
Mouth	Halitosis, toothache and gingivitis after tooth extraction, dry and thirsty, bitter taste, taste as from bad eggs (Tyler, 1992; Vermeulen, 1997; Vithoulkas, 1995).

Throat	Acute tonsillitis, dysphagia, swelling of soft palate and uvula (Vermeulen, 1997; Vithoulkas, 1995).
Stomach	Canine hunger, haematemesis after trauma, eructations, anorexia, fetid breath, diabetes, disorders of taste and thirst, craving for vinegar, aversion to milk and meat, feeling as if stomach was pressing against spine (Vermeulen, 1997; Vithoulkas, 1995).
Abdomen	Hard distension, colic, nausea, bruised pains on the sides of the ribs (Vermeulen, 1997; Vithoulkas, 1995).
Rectum	Tenesmus in diarrhoea, prolapsus ani, dysentery; offensive, brown, bloody, putrid, involuntary stool, looks like brown yeast (Vermeulen, 1997; Vithoulkas, 1995), flatus smells like rotten eggs (Vithoulkas, 1995).
Urinary	Urinary retention from overexertion and after labour, vesical tenesmus, involuntary dribbling, constant urging, haematuria from mechanical causes (Tyler, 1992; Vermeulen, 1997; Vithoulkas, 1995).
Male	Impotence from sexual excess or abuse, phimosis from friction, haematocele, swelling of penis and scrotum after trauma (Tyler, 1992; Vermeulen, 1997; Vithoulkas, 1995).
Female	Sore, lame and bruised parts after labour especially after caesarean; uterine haemorrhage from mechanical trauma and after coition, mastitis from trauma, threatened abortion from falls, puerperal fever and tumours of breasts from injury (Tyler, 1992; Vermeulen, 1997; Vithoulkas, 1995).
Respiratory	Hoarseness of voice from overuse, bronchitis, pleurodynia; paroxysmal coughs at night, during sleep, worse for exercise (Vermeulen, 1997); whooping cough and dyspnoea; cough produced by weeping and lamenting (Vermeulen, 1997; Vithoulkas, 1995); haemoptysis, pneumothorax or pleurisy after trauma (Tyler, 1992).
Heart	Angina pectoris; cardiac dropsy, dyspnoea, fatty heart, hypertrophy of the heart, palpitations on least exertion, weak heart muscle, pressure under sternum, anguish and collapse (Vermeulen, 1997).
Back	Soreness and pain on the back, neck, between the scapulae and from last rib to axilla at every inspiration (Vermeulen, 1997; Vithoulkas, 1995).
Extremities	Gout, great fear of being touched or approached; trauma, soreness after

	overexertion, rheumatism, coldness of extremities, writer's cramp, sciatica, hygroma patellae, numbness of feet, heaviness of limbs, paralysis, lumbago, sprain, cracking and sensation of dislocation on wrist during movement (Tyler, 1992; Vermeulen, 1997; Vithoulkas, 1995).
Sleep	Insomnia because the bed feels too hard (Vermeulen, 1997; Vithoulkas, 1995) and restless when overtired, comatose drowsiness, dreams of graves and striking lightning, ghosts, spirits, black animals, death, injured bodies and black forms of spectres (Vermeulen, 1997), of being buried alive, funerals, suffocation (Vithoulkas, 1995).
Skin	Abscess, bed sores, crops of small boils, bruises, carbuncles, ecchymosis black and blue, excoriations, sore nipples, wounds, small pimples, acne, petechiae, erysipelas, insect bites, eruption after trauma and scarlet fever when eruption does not come out (Vermeulen, 1997; Vithoulkas, 1995).
Fever	Petechial fever, typhoid fever and traumatic fever; heat and redness of head, with coolness of rest of body; internal heat, feet and hands cold; nightly sour sweats (Tyler, 1992; Vermeulen, 1997; Vithoulkas, 1995).

2.8 Related research

Similar *in vitro* studies were conducted at the University of Johannesburg. Bengsch (2000) and Vermeulen (2000) conducted similar studies to investigate the effect of *Arnica montana* 30C and mother tincture on blood coagulation by measuring Prothrombin Time and activated Partial Thromboplastin Time. The results of these studies showed lowered coagulability of blood, but there was no statistically significant difference between the experimental and the control group. Hohl (2005) and van Tonder (2005) conducted two similar studies to investigate whether *Arnica montana* D2, D6, 30C and 200C potencies cause fibrinolysis by measuring the D-dimers after treating a blood clot with *Arnica montana in vitro*. The results of these two studies did not show any presence of D-dimers. Bengsch (2000), Vermeulen (2000), Hohl (2005) and van Tonder (2005) suggested that similar studies should be repeated *in vivo* on subjects taking homeopathic *Arnica montana* as homeopathy focuses on the entire individual and how the individual reacts as a totality. The results of the first two studies offer persuasive evidence in support of hypothesis of this study due to the coagubility effect shown with the *Arnica montana* 30C and mother tincture.

Brinkhause *et al.* (2006), investigated the effectiveness of homeopathic *Arnica montana* D30 on postoperative swelling and pain after arthroscopy, artificial knee joint implantation, and cruciate ligament reconstruction (CLR). Patients receiving homeopathic *Arnica montana* D30 in all three trials showed a trend towards less postoperative swelling compared to patients receiving placebo. However, a statistically significant difference between experimental and control group in favour of homeopathic *Arnica montana* D30 was only found in the CLR trial. This conclusion has shown promising results for the treatment of post operative swelling but as mentioned earlier research needs to be conducted on the use of *Arnica montana* 6C before surgery to ensure that there is no increased risk of post operative haemorrhage.

Oberbaum *et al.* (2003), conducted a double blind, placebo-controlled, randomised, clinical trial on *Arnica montana* 6C, 30C and *Bellis perennis* 6C, 30C to evaluate their effect on postpartum blood loss. Forty pregnant participants were randomised to one of three groups: *Arnica montana* 6C and *Bellis perennis* 6C, *Arnica montana* C30 and *Bellis perennis* C30, or double placebo. After forty-eight hours the *Arnica montana* 6C, 30C/placebo was halted, and patients continued the *Bellis perennis* 6C, 30C/placebo until cessation of lochia.

In seventy-two hours after giving birth, the mean haemoglobin (Hb) levels remained similar after treatment with homeopathic remedies as compared to a significant decrease in Hb levels in the placebo group. It was concluded that the treatment with homeopathic *Arnica montana* 6C, 30C and *Bellis perennis* 6C, 30C may reduce postpartum blood loss, as compared with placebo (Oberbaum *et al.,* 2003). This conclusion has shown support to the hypothesis of this study as there was less bleeding after surgery.

CHAPTER 3

METHODOLOGY

3.1 Sample group

This was a double-blind, placebo-controlled study. A total sample group for this three part study consisted of eighty healthy participants between the ages of eighteen to thirty five. They were from both genders, belonged to different socio-economic levels and were from different ethnic groups. Participants were recruited by means of poster advertising at the University of Johannesburg (UJ) Health Training Centre (Appendix A). The eighty participants were allocated a participant number and randomised by the research supervisor into four groups of twenty participants. Twenty participants were in the placebo group that was shared by all three studies. Twenty participants were allocated to the experimental group for this study. The study was conducted over a period of two weeks at the UJ Doornfontein Campus Homeopathy Health Centre.

3.1.1 Exclusion criteria

The participants that were diagnosed with and/or suffer from the following conditions were excluded from the study as these conditions may have had an impact on the results of the study:

- Hypertension
- Hypotension
- Heart disease
- A bleeding disorder
- Anaemia
- Iron or any vitamin deficiency
- Liver disease
- Malaria
- Currently on aspirin or anticoagulants

3.2 Preparation of remedies

The remedies were prepared by Natura Laboratory in Pretoria. The remedies *Arnica montana* 6C were prepared in 20% ethanol. The placebo had no medicine in it and it consisted of 20% ethanol only. These were prepared according to the standard homeopathic manufacturing procedures. *Arnica montana* 6C and the placebo were both bottled the same in 25mL amber glass bottles. The bottles were labelled in numbers to blind the participants from knowing the contents of their bottles.

3.3 Research procedure and design

Interested participants were invited to the Homeopathy Health Centre for an initial consultation. The initial consultation included: an explanation of the aims of the study and research procedure, participants were requested to sign an Information and Consent Form (Appendix B), a full Case History was taken and Physical Examination was performed (Appendix C). Participants that fulfilled the inclusion criteria were then requested to come to the Homeopathy Health Centre again for blood sampling and to have their Bleeding Times measured.

The Bleeding Times and the blood sampling were done on the first day of the two-week duration of the study. The Bleeding Time measurements were done by first cleaning the area that is to be cut with an alcohol swab. The blood pressure cuff was placed on the upper arm and inflated to 40 mm Hg. An automatic, spring-loaded lancet was used to make a standard-sized cut on the underside of the forearm. The area stabbed was selected so that no superficial or visible veins are cut. A filter paper was used to blot the blood at the edges of the cut and not on top of the wound (without touching the wound). The time from when the stab wound was made until all bleeding had stopped was measured and this was recorded as the Bleeding Time.

A trained phlebotomist then drew 20mL of venous blood from each participant for analysis. These blood samples were drawn into blue top vacutainer tubes containing 3.2% of trisodium citrate. After the first blood samples were taken, the participants (depending on their participant number allocated by the research supervisor) were either given a 25mL bottle of *Arnica montana* 6C in 20% ethanol or an identical bottle of 20% ethanol (placebo). Participants were provided with a "How to take your Medication" Leaflet (Appendix D) that explained the dosage: ten drops under the tongue twice a day for fourteen days, as well as special storage instructions. The blood samples were taken to

Johannesburg Hospital Haematology Laboratory immediately by the researcher for aPTT and PT coagulation studies.

Follow-up consultations were scheduled seven and fourteen days after initiating treatment. At both follow-up consultations another focussed case history and physical examination were performed. After the second follow-up consultation the Bleeding Times were measured and fresh venous samples were drawn by the phlebotomist and sent away for the same coagulation studies as described above.

3.3.1 Running of tests

The tests were performed within 6 hours of sample collection. During this time the samples were kept at 4°C. The tests were performed on the platelet poor plasma. The samples were centrifuged at 3000rpm for 15 minutes to obtain the platelet poor plasma.

The Prothrombin Times were done by placing all reagents in their correct positions. De-capped primary specimen tubes were placed in the specimen rack with the barcodes clearly visible on the outside. Once the analyser was programmed with appropriate tests, the analyser was started. When the tests were completed, a small "v" appeared next to the sample indicating that the test is completed and validated. The results from the analyser were downloaded automatically to the host computer. The results were expressed in both seconds and International Normalised Ratio (INR). Prior to accepting the results, the control was ensured to be within acceptable limits.

The activated Partial Thromboplastin Time procedures were performed within 4 hours of sample collection and were kept at 4° C. 0.1mL of plasma was added into glass tubes. 0.1mL of aPTT reagent was added and incubated at 37° C for 5 minutes. After 5 minutes, 0.1mL of calcium chloride was added and the stopwatch was started. The time taken for the clot to form was recorded. The mean clotting time obtained was recorded in seconds. The time obtained for the participant and the normal control were both reported and were interpreted. These studies were supervised by Dr Mahlangu (specialist supervisor), a haematologist at Johannesburg Hospital.

3.4 Medication administration

After withdrawing the first blood samples, the participants (depending on their participant number allocated by the research supervisor) were either given a 25mL bottle of *Arnica montana* 6C in 20% ethanol or an identical bottle of 20% ethanol (placebo). Participants were provided with a "How to take your Medication" Leaflet (Appendix D) that explained the dosage: ten drops under the tongue twice a day for fourteen days as well as special storage instructions. Participants were also given a compliance leaflet to record the administration of each dose.

3.5 Reliability and validity measures

The remedies were purchased from Natura Laboratory in Pretoria and they were all from the same batch number. The participants were requested not to make changes to their lifestyles and requested to abstain from consuming alcohol for the duration of the trial. Blood samples were taken by a trained phlebotomist. The aPTT and PT tests are performed each day in the laboratory using standard protocols. The laboratory reagents were checked using commercial controls before the tests were run. The Bleeding Times (BT) were done by trained medical technologists as per procedure explained above. These studies were supervised by Dr Mahlangu (specialist supervisor), a haematologist at Johannesburg General Hospital.

3.6 Data collection and analysis

The Bleeding Times were taken and recorded on the first day and on the last day of the two weeks of the study. The PT and aPTT were performed on the first and second blood samples. The results of the experimental group were also compared to those of the control group. These results were analysed using ordinary descriptive statistics such as frequencies, percentages, mean and standard deviation. The results that were obtained before medication were compared to the results obtained after medication. Changes over time in Prothrombin Time, activated Partial Thromboplastin Time and Bleeding Time were ascertained utilising ANOVA (analysis of variance) (Van Staden, 2008).

3.7 Ethical considerations

Each participant was given a participant number for confidentiality and anonymity. The consent form that participants signed informed them that their participation in the study was voluntary, that they could withdraw at any time and that there could be discomfort or pain during the withdrawal of blood. All information was kept strictly confidential and only the researcher and research supervisor had access to participant files. There were no anticipated risks or side effects associated with *Arnica montana* 6C and participants were monitored on a weekly basis to ensure that there were no undesirable reactions to the medication. The participants had the contact number of the researcher and research supervisor in case they encountered any problem during the period of medication. In that instance the participants would be told to stop the medication immediately, would be withdrawn from the study if necessary and referred accordingly. The findings of the study were made available to the participants on request.

CHAPTER 4

RESULTS

4.1 Introduction

The results of the experimental group were compared to those of the control group on both the first (INR1, aPTT1 and BT1) and second tests (INR2, aPTT2 and BT2). The results that were obtained from the first tests before medication were also compared to the results obtained from the second tests after medication. The results from different groups of the three part study were also compared together. The results were analysed using ordinary descriptive statistics such as frequencies, percentages, mean and standard deviation. Changes over time in PT, aPTT and BT were ascertained utilising ANOVA (analysis of variance).

4.2 Result analysis

4.2.1 Comparisons between the experimental and control group in INR, aPTT and BT.

The Kolmogorov and Sharpiro-Wilk Tests were used to test the normality between experimental and the control group in INR, aPTT and BT. The two groups were found to be comparable to each other. This is indicated in Table 4 and the p-value of more than 0.05 means that there is no statistically significant difference between the experimental and control group. The p-values that were less than 0.05 were only seen in aPTT2 of both the experimental and control group. This showed a statistically significant difference in aPTT2.

Table 4. Tests of Normality

Tests of Normality

	Group	Kolmogorov-Smirnov(a)			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
INR1	***Arnica montana* 6C**	0.146	20	0.200(*)	0.965	20	0.640
	Placebo	0.190	19	0.070	0.949	19	0.382
aPTT1	***Arnica montana* 6C**	0.136	20	0.200(*)	0.934	20	0.181
	Placebo	0.161	19	0.200(*)	0.941	19	0.274
BT1	***Arnica montana* 6C**	0.174	20	0.113	0.901	20	0.042
	Placebo	0.132	19	0.200(*)	0.945	19	0.323
INR2	***Arnica montana* 6C**	0.176	20	0.107	0.931	20	0.163
	Placebo	0.122	19	0.200(*)	0.982	19	0.961
aPTT2	***Arnica montana* 6C**	0.298	20	0.000	0.790	20	0.001
	Placebo	0.210	19	0.027	0.843	19	0.005
BT2	***Arnica montana* 6C**	0.143	20	.0200(*)	0.952	20	0.395
	Placebo	0.170	19	0.152	0.907	19	0.066

* This is a lower bound of the true significance

a Lilliefors Significance Correction

The Independent Samples t-tests (Lavene's test and T-Test for equality of means) and Mann-Whitney were used to determine if there was any statistical significant difference between the experimental and control group in INR, aPTT and BT. The results indicated that there was no significant difference. Table 5 also indicates that all the p-values were greater than 0.05 except for INR1 in Lavene's Test for Equality of Variances.

Table 5. T-tests comparing experimental and control group before and after medication.

Test	Lavene's Test	T-Test For equality of means	Mann-Whitney U	Wilcoxon W	Z	Asymp. Sig. (2-tailed)	Exact sig. [2*(1-tailed)]
INR1	0.141	0.485	159.500	369.500	-1.100	0.271	0.277(a)
aPTT1	0.621	0.042	120.000	330.000	-2.165	0.030	0.030(a)
BT1	0.655	0.854	195.000	405.000	-0.135	0.892	0.904(a)
INR2	0.302	0.573	170.000	380.000	-0.564	0.573	0.588(a)
aPTT2	0.774	0.028	92.000	282.000	-2.757	0.006	0.005(a)
BT2	0.307	0.172	146.000	356.000	-1.237	0.216	0.224(a)

a Not corrected for ties.

The Multiple Box-and-Whisker plots below were also used to illustrate whether there were significant differences between the experimental and control group in INR, aPTT and BT.

Figure 3. Comparison between the experimental and control group in INR1 and INR2.

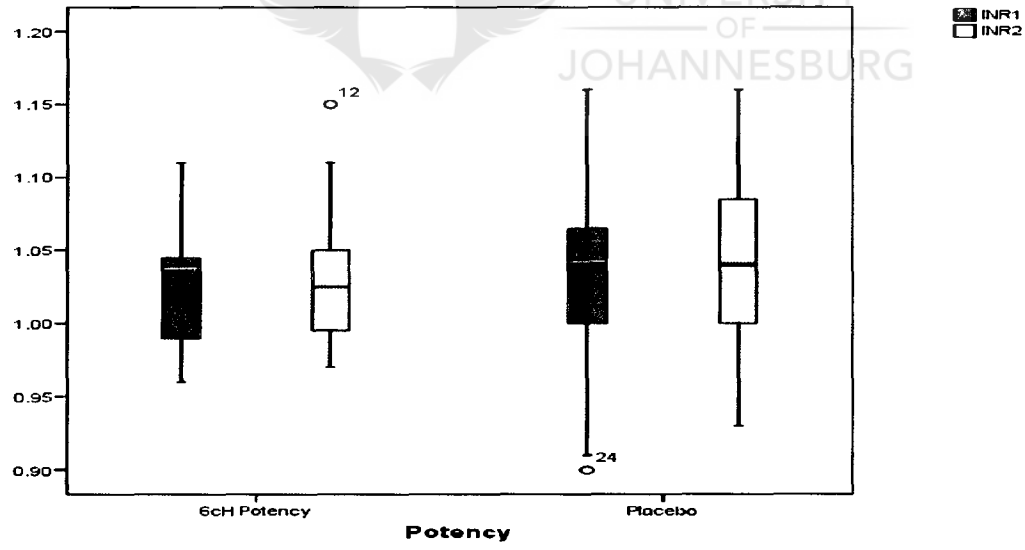

Figure 3 shows that the experimental group had a median INR1 of 1.0150 and the control group had 1.0400. Therefore there was no significant difference in INR1 between the experimental and the control group. The experimental group also had a median INR2 of 1.0250 and the control group had 1.0400. Therefore there was no significant difference in INR2 between the experimental and the control group.

Figure 4. Comparison between the experimental and control group in aPTT1 and aPTT2.

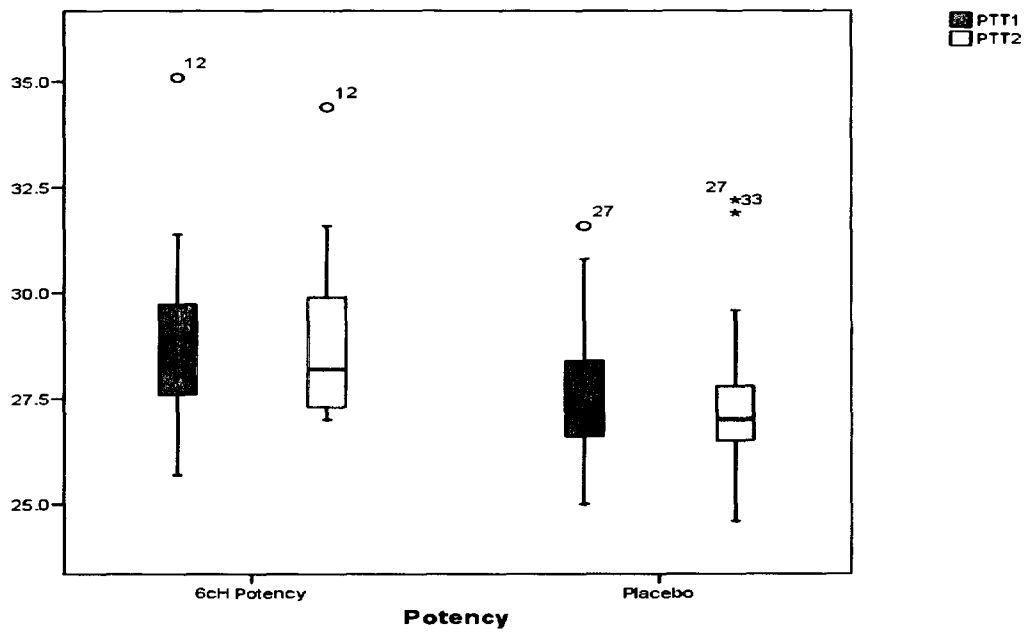

Figure 4 shows that the experimental group had a median aPTT1 of 28.950 and the control group had 27.150. Therefore there was no significant difference in aPTT1 between the experimental and the control group. Figure 4 also shows that the experimental group had a median aPTT2 of 28.2000 and the control group had 27.0000. Therefore there was no significant difference in INR2 between the experimental and the control group.

Figure 5. Comparison between the experimental and control group in BT1 and BT2.

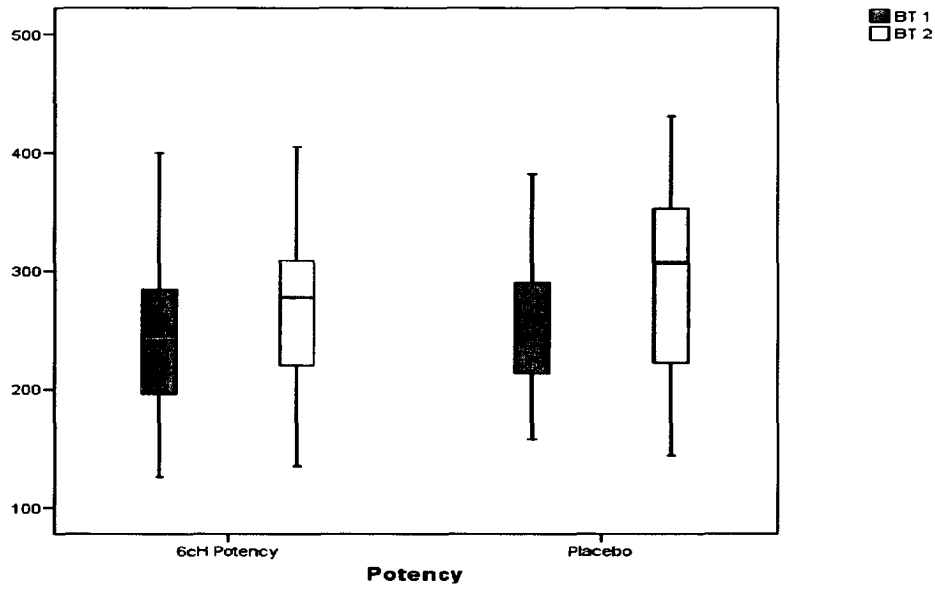

Figure 5 shows that the experimental group had a median BT1 of 251.50 and the control group had 245.50. Therefore there was no significant difference in BT1 between the experimental and the control group. Figure 5 also shows that the experimental group had a median BT2 of 278.00 and the control group had 307.00. Therefore there was no significant difference in INR2 between the experimental and the control group.

4.2.2 Comparison between the first tests before medication and the second tests after medication.

The Paired Samples T-Test and the Wilcoxon Signed Ranks Test were used to determine the significant difference between the first tests before medication and the second tests after medication.

Table 6. Paired Samples Test.

			Paired Differences					t	df	Sig. (2-tailed)
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		Mean	Std. Deviation	Std. Error Mean
			Lower	Upper	Lower	Upper	Lower	Upper	Lower	Upper
***Arnica montana* 6C**	**Pair 1**	**INR1 - INR2**	-0.01200	0.04652	0.01040	-0.03377	0.00977	-1.154	19	0.263
	Pair 2	**aPTT1 - aPTT2**	0.00000	1.19605	0.26744	-0.55977	0.55977	0.000	19	1.000
	Pair 3	**BT 1 - BT 2**	-15.900	79.687	17.819	-53.195	21.395	-0.892	19	0.383
Placebo	**Pair 1**	**INR1 - INR2**	-0.01368	0.05590	0.01282	-0.04063	0.01326	-1.067	18	0.300
	Pair 2	**aPTT1 - aPTT2**	0.19474	1.46571	0.33626	-0.51171	0.90119	0.579	18	0.570
	Pair 3	**BT 1 - BT 2**	-44.368	78.566	18.024	-82.236	-6.501	-2.462	18	0.024

Table 6 showed that there was no significant difference in the p-values of the experimental and control group except for the Bleeding Time in the control group. Therefore there was a significant difference between BT1 and BT2 in the control group.

Table 7. Wilcoxon Signed Rank Test

Test Statistics(c)

		INR2 - INR1	aPTT2 - aPTT1	BT 2 - BT 1
***Arnica montana* 6C**	**Z**	-0.641(a)	-.112(b)	-1.083(a)
	Asymp. Sig. (2-tailed)	0.521	0.911	0.279
Placebo	**Z**	-0.805(a)	-.479(b)	-2.335(a)
	Asymp. Sig. (2-tailed)	0.421	0.632	0.020

a Based on negative ranks.

b Based on positive ranks.

c Wilcoxon Signed Ranks Test

Table 7 also showed that there was no significant difference in all the p-values except in the difference between BT2 and BT1 in the control group. Therefore there was a significant difference between BT2 and BT1 in the control group.

4.2.3 Comparison between *Arnica montana* 6C, 30C, complex and control group.

A total sample group for this three part study consisted of eighty participants. These eighty participants were randomised by the research supervisor into four groups. Twenty participants were in the placebo group that was shared by all three studies. Sixty participants were allocated to the experimental group. The experimental group consisted of three groups of twenty participants. The three different groups differed with the remedies that each group was taking which were *Arnica montana* 6C, *Arnica montana* 30C and a complex remedy. The complex remedy consisted of *Arnica montana* 6C, *Arnica montana* 30C and *Arnica montana* 200C. These four groups were compared to see if there was any significant difference between them. This is illustrated below in the following tables.

Table 8. Test of Normality

	Group	Kolmogorov-Smirnov(a)			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
INR1	6cH potency	0.097	20	0.200(*)	0.962	20	0.590
	30cH potency	0.147	20	0.200(*)	0.927	20	0.136
	Placebo	0.150	20	0.200(*)	0.961	20	0.563
	Complex remedy	0.203	20	0.030	0.965	20	0.644
aPTT1	6cH potency	0.138	20	0.200(*)	0.920	20	0.100
	30cH potency	0.106	20	0.200(*)	0.979	20	0.924
	Placebo	0.148	20	0.200(*)	0.925	20	0.125
	Complex remedy	0.111	20	0.200(*)	0.944	20	0.288
BT1	6cH potency	0.119	20	0.200(*)	0.941	20	0.254
	30cH potency	0.191	20	0.055	0.910	20	0.065
	Placebo	0.120	20	0.200(*)	0.949	20	0.348
	Complex remedy	0.097	20	0.200(*)	0.975	20	0.852
INR2	6cH potency	0.153	20	0.200(*)	0.925	20	0.122
	30cH potency	0.192	20	0.052	0.938	20	0.217
	Placebo	0.145	19	0.200(*)	0.961	19	0.591
	Complex remedy	0.148	20	0.200(*)	0.978	20	0.910
aPTT2	6cH potency	0.126	20	0.200(*)	0.972	20	0.793
	30cH potency	0.110	20	0.200(*)	0.959	20	0.519
	Placebo	0.141	19	0.200(*)	0.944	19	0.305
	Complex remedy	0.179	20	0.092	0.923	20	0.113
BT2	6cH potency	0.143	20	0.200(*)	0.952	20	0.395
	30cH potency	0.131	20	0.200(*)	0.963	20	0.614
	Placebo	0.170	19	0.152	0.907	19	0.066
	Complex remedy	0.138	20	0.200(*)	0.941	20	0.253

a Lilliefors Significance Correction

* This is a lower bound of the true significance.

The Kolmogorov and Sharpiro-Wilk Tests were used to test the normality between experimental groups (*Arnica montana* 6C, 30C and Complex remedy) and the control group in INR, aPTT and BT. The four groups were found to be comparable to each other. This is indicated in Table 8 and the p-value of more than 0.05 means that there is no significant difference between the four groups.

The p-values of less than 0.05 were only seen in INR1-Complex remedy in Kolmogov-Smirnov Test and this showed a significant difference in the INR1 of the Complex remedy.

Table 9. One Way Analysis of Variances.

	Lavene's Test	**ANOVA**	**Robust Test of equality of means**	**Kruskal-Wallis Test**
INR1	0.274	0.887	0.887	0.756
aPTT1	0.781	0.084	0.085	0.095
BT1	0.187	0.984	0.984	0.946
INR2	0.273	0.790	0.791	0.688
aPTT2	0.242	0.097	0.099	0.054
BT2	0.726	0.425	0.426	0.551

Table 9 shows the tests that were used to see if there was a significant difference in the four groups in INR, aPTT and BT before and after medication. The p-values were all greater than 0.05, therefore there was no significant difference between the groups.

Table 10. Paired Samples Test

Potency			Paired Differences					t	df	Sig. (2-tailed)
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		Mean	Std. Deviation	Std. Error Mean
						Lower	Upper	Lower	Upper	
6cH Potency	Pair 1	INR1 - INR2	-0.01200	0.04652	0.01040	-0.03377	0.00977	-1.154	19	0.263
	Pair 2	aPTT1 - aPTT2	0.00000	1.19605	0.26744	-0.55977	0.55977	0.000	19	1.000
	Pair 3	BT 1 - BT 2	-15.900	79.687	17.819	-53.195	21.395	-0.892	19	0.383
30cH Potency	Pair 1	INR1 - INR2	-.01750	0.04962	0.01109	-0.04072	0.00572	-1.577	19	0.131
	Pair 2	aPTT1 - aPTT2	0.40000	1.49349	0.33396	-0.29898	1.09898	1.198	19	0.246
	Pair 3	BT 1 - BT 2	-11.750	90.327	20.198	-54.024	30.524	-0.582	19	0.568
Complex Remedy	Pair 1	INR1 - INR2	-0.01300	0.02886	0.00645	-0.02650	0.00050	-2.015	19	0.058
	Pair 2	aPTT1 - aPTT2	-0.45000	2.44271	0.54621	-1.59322	0.69322	-0.824	19	0.420
	Pair 3	BT 1 - BT 2	-37.150	91.615	20.486	-80.027	5.727	-1.813	19	0.086
Placebo	Pair 1	INR1 - INR2	-0.01368	0.05590	0.01282	-0.04063	0.01326	-1.067	18	0.300
	Pair 2	aPTT1 - aPTT2	0.19474	1.46571	0.33626	-0.51171	0.90119	0.579	18	0.570
	Pair 3	BT 1 - BT 2	-44.368	78.566	18.024	-82.236	-6.501	-2.462	18	0.024

The Paired Samples Test was also used to see if there was a significant difference in the four groups in INR, aPTT and BT before and after medication. The p-values were all greater than 0.05, therefore there was no significant difference between the groups. An exception was seen in the difference between BT2 and BT1 in the control group. Therefore there was a significant difference between BT2 and BT1 in the control group.

4.3 Study compliance

All twenty participants in the experimental group completed the study and were included in the analysis of the results. One participant in the control group withdrew from the study due to personal

reasons and this participant was excluded from the analysis of the results. Adherence to the treatment was good and no participants were excluded from the study due to non-adherence to medication.

4.4 New symptoms

Six participants from the experimental group reported to have experienced some new symptoms during the medication period. These symptom were, slight bleeding of tongue during brushing of it (1), deep cut on finger that had difficulty healing and the participant felt that it took long to stop bleeding (1), headaches (3), dizziness (2), clear and watery coryza (1), body and joint pains (4), fatigue (3), aching muscles (4), flatulence (3), colic and dyspepsia (2) (The numbers next to the above symptoms indicate the number of participants that experienced that symptom).

CHAPTER 5

DISCUSSION OF RESULTS

5.1 Introduction

In this three part study, eighty participants were randomised into four groups of twenty participants. Twenty participants were in the placebo group that was shared by all three studies. Twenty participants were allocated to the experimental group for this study and they were given *Arnica montana* 6C. The study was conducted over a period of two weeks at the UJ Doornfontein Campus Homeopathy Health Centre.

The Bleeding Times were taken and recorded on the first day and on the last day of the two weeks of the study. The Prothrombin Time and activated Partial Thromboplastin Time were performed on the first and second blood samples. The results of the experimental group were also compared to those of the control group. These results were analysed using ordinary descriptive statistics such as frequencies, percentages, mean and standard deviation. The results that were obtained before medication were compared to the results obtained after medication. Changes over time in Prothrombin Time, Activated Partial Thromboplastin Time and Bleeding Time were ascertained utilising ANOVA (analysis of variants).

5.2 Summary of results

5.2.1 Comparisons between the experimental and control group in INR, aPTT and BT.

The Independent Samples t-tests (Lavene's test and t-Test for equality of means) and Mann-Whitney were used to determine if there was any statistically significant difference between the experimental and control group in INR, aPTT and BT. The results indicated that there was no statistically significant difference in the median INR and BT of the experimental and control group. The p-values of aPTT1 and aPTT2 were less than 0.05 in the Independent Samples t-test (t-test for equality of means) and Mann-Whitney Test [Asymp. Sig. (2-tailed), Exact sig.[2*(1-tailed)]]. This means that there was no difference in blood coagulation times between the control and the experimental

group as measured by PT and BT. These results suggest that *Arnica montana* 6C does not prolong blood coagulation.

5.2.2 Comparison between the first tests before medication and the second tests after medication.

The Paired Samples t-Test and the Wilcoxon Signed Ranks Test were used to determine the statistically significant difference between the first tests before medication and the second tests after medication. These tests showed that there was no significant difference in all the p-values except for the Bleeding Time in the control group. Therefore there was a statistically significant difference between BT1 and BT2 in the control group. This means that there was no significant change in blood coagulation times as measured by PT, aPTT and BT after *Arnica montana* 6C was administered to the participants.

5.2.3 Comparison between *Arnica montana* 6C, 30C, complex and control group.

These four groups were compared to see if there was any statistically significant difference between them. These groups were found to be comparable to each other. The p-values were greater than 0.05 and this meant that there was no statistically significant difference between the four groups. The p-values of less than 0.05 were only seen in INR1-Complex remedy in Kolmogov-Smirnov Test and this showed a statistically significant difference in the INR1 of the Complex remedy. This means that the three experimental groups and the control group did not differ in blood coagulation times. This confirms the hypothesis that *Arnica montana* does not prolong blood coagulation.

5.3 Placebo effect

The results of this study showed a statistically significant difference in the placebo group only in median BT2. This indicated the Bleeding Time influence that the placebo effect has. This means that an inert substance can prolong the Bleeding Time.

CHAPTER 6

CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The results that were found during this study support the hypothesis that *Arnica montana* 6C does not have an effect on blood coagulation as measured by Prothrombin (PT), activated Partial Thromboplastin (aPTT) and Bleeding Times (BT). This evidence supporting the hypothesis is very valuable when considering the possible therapeutic value of using homeopathic *Arnica montana* post operatively. The previous lack of research evidence to reduce the concerns regarding the risks of increased bleeding associated with herbal preparations of *Arnica Montana* has had a negative impact on the application of this valuable therapeutic tool. The results of this research study can be used in support of utilising *Arnica Montana* 6C before surgery without increasing the risk of post-operative haemorrhage.

6.2 Recommendations

The following advises are recommended to improve quality of the study:

- The size of the sample group could be increased to decrease the margin of sample group and to make statistical interpretation more accurate.
- The trial period could be made shorter to maximise the adherence to treatment.
- Human participants could be exchanged with animals like rats or pigs to have a more controlled environment, to ensure compliance and adherence to treatment.
- More experienced laboratory personnel could be used to reduce errors especially in Bleeding Time measurement.
- The study could include only one gender to eliminate possible gender differences in blood coagulation.

- A combination of other homeopathic remedies with *Arnica montana* could be studied.

- The study could be done on participants who are about to undergo a surgical procedure.

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APPENDICES

APPENDIX A

STUDY POSTER ADVERTISEMENT

UNIVERSITY OF JOHANNESBURG

Research Study

Are you healthy and between the ages of 18 and 35

We are looking for volunteers to participate in a research study on the effect of homoeopathically prepared *Arnica montana* on blood coagulation.

This research study has been approved by the Faculty of Health Sciences Higher Degrees and Ethics Committee on (Number …..).

If you are interested please contact:

Thobela Nkunjana on 083 491 5687

Research Supervisor : Dr Brenda Saunders (011 559 6599)

APPENDIX B

PARTICIPANT INFORMATION AND CONSENT FORM

Dear Participant,

My name is Thobela Nkunjana. I am doing a Masters Degree in Homeopathy at the University of Johannesburg. I am doing a research study as a partial fulfillment of my degree. The purpose of this study is to determine the effect of the homoeopathically prepared *Arnica montana* 6C on blood coagulation. *Arnica montana* 6C is a homoeopathic remedy which is sometimes prescribed clinically in the treatment of traumatic injury and post operative bruising. You are invited to participate in this study.

In order to participate in this study, you must be healthy and between the ages of 18 and 35. You can not participate in this study if you have any of the following:

- If you are currently taking aspirin, anti-coagulants, or any other conventional or complementary medication that could interfere with blood coagulation
- If you have been diagnosed with any of the following conditions: high blood pressure, low blood pressure, heart disease, bleeding disorders, iron or any vitamin deficiency, anaemia, liver disease and malaria.

This study forms part of a three part study to determine the effect of *Arnica montana* homoeopathic preparations on blood coagulation. This study will investigate the effect of *Arnica montana* 6C on these measurements. The total sample group for my study will consist of forty participants. This is a double blind, placebo controlled trial. You will be allocated a participant number by the research supervisor and will be placed either in the experimental group where you will given *Arnica montana* 6C or in the control group where you will be given a non active placebo.

The study will be conducted over a period of two weeks at the UJ Doorfontein Campus Homeopathy Health Centre. Your initial consultation will include an explanation of the aims of the study and research procedure, signing this Information and Consent Form, a full Case History and Physical Examination will be performed. A trained phlebotomist will then draw 20mL of venous blood for analysis at the haematology laboratory in Johannesburg Hospital .

Medicine administration

After donating the first blood samples you will be given a 25ml bottle of *Arnica montana* 6C in 20% ethanol or an identical bottle of 20% ethanol (placebo). Participants will be provided with a "How to take your Medication" leaflet that explains the dosage as well as special storage instructions.

Follow up consultations

Follow up consultations will be scheduled seven and fourteen days after initiating treatment. At both followup consultations another case history will be taken and a physical examination performed. After the second follow up consultation another venous sample will be drawn by the phlebotomist and sent away for the same coagulation studies. The researcher will also measure the Bleeding Time.

There are no anticipated side effects in this study but there may be slight discomfort during the venipuncture procedure. You will be given the contact number of the researcher and research supervisor in the unlikely event of you encountering any problem during the period of medication. In this case you will be told to stop the medication immediately and will be withdrawn from the study.

Your participation in this study is completely voluntary and you can withdraw from the study at any time. All data collected during the research procedure will be kept strictly confidential and no identifying data will be published in the research dissertation. Participant files will be kept under lock and key at the University of Johannesburg Homeopathy Health Centre and only the researcher and research supervisor will have access to these files. Your participation is very important, as it will contribute significantly to the homoeopathic research.

I,----------, understand the purpose and the methods that will be used in this study. I also understand that there may be some pain and discomfort when the phlebotomist draws blood from my arm.

I agree □ I disagree □ to take part in this study.

Signature:..... Date:.....

I, the researcher, have explained the purpose and the methods that will be used in this study. I have explained that there may be some pain and discomfort when the phlebotomist draws blood from the arm. I also have explained that the study is voluntary and that the volunteer can withdraw from the study any time.

Signature:..... Date:.....

EMERGENCY NUMBERS:

Researcher: Thobela Nkunjana: 083 491 5687

Research supervisor: Dr B. Saunders: 011 559 6599 (084 424 6364)

APPENDIX C

UNIVERSITY OF JOHANNESBURG

HOMEOPATHY HEALTH CENTRE

RESEARCH SCREENING QUESTIONNAIRE AND CASE TAKING FORM

For office use only.
Participant Number:.....

Personal Information

Date: _____ Time: _____

Name _____ Date of Birth:_____Age:_____

Marital Status: Single/Married/Divorced/Separated/Widowed/Co-habiting Sex:_____

Occupation: _____ Address:_____

_____

Contact Tel Number:

Screening Questionnaire

1. Have you ever been diagnosed with each of the following conditions? Please mark (X) all applicable.

□ Hypertension
□ Hypotension
□ Bleeding disorder (please specify).....
□ Anaemia (please specify).....
□ Heart disease (please specify).....
□ Vitamin deficiency (please specify).....
□ Iron deficiency.....
□ Liver disease (please specify).....

2. Do you bleed or bruise easily Y / N (if yes, please specify)?.....

.....

3. Do you suffer from uncontrollable or spontaneous bleeding Y / N (if yes, please specify)?

.....

4. Are you currently on any medication Y / N (if yes, please specify)?.....

.....

5. Are you currently taking aspirin Y / N ?

If yes:

- Why?.....
- Daily dosage?.....

6. Do you drink alcohol Y / N ?

If yes:

- What do you drink (e.g. beer, wine, spirit etc.)?.....
- How many units do you drink per week? - give categories

.....

7. Do you smoke Y / N ?

If yes:

- What do you smoke? cigars/cigarettes.....
- On average how many do you smoke per day?.....

8. Have you visited a malaria area in the last year Y / N ? If yes what date?

.....

If yes, have you been diagnosed with malaria Y / N ?

9. Have you had any illnesses in the last six months Y / N ? If yes please specify.

.....

For office use only

DOES THE PARTICIPANT SATISFY THE INCLUSION CRITERIA FOR THIS STUDY? Y / N

If No, for which reasons is the volunteer excluded from the study?

.....

If participant meets inclusion criteria continue with case taking

Past History

General state of health: _____

Childhood ilnesses:_____

Operations/Hospitalisations:

_____

_____

Current Medications:

_____

_____

Allergies:_____

_____

Immunisations:_____

Diet:_____

_____

_____

Drugs:_____

Social History

Family History

System Review

Enquire about common symptoms and three or four of the common disorders in each major system:
Cardiovascular system
Have you had any pain or pressure in your chest, neck or arm?
Are you short of breath on exertion? How much exertion is necessary?
Have you ever woken up at night short of breath?
Can you lie flat without feeling breathless?
Have you had swelling of your ankles?
Have you noticed your heart racing or beating irregularly?
Do you have pain in your legs on exercise?
Do you have cold or blue hands or feet?
Have you ever had rheumatic fever, a heart attack, or high blood pressure?
Respiratory system
Are you ever short of breath?
Have you had any cough?
Do you cough up anything?
Have you coughed up blood?
Do you snore loudly?
Do you ever have wheezing when you are short of breath?
Have you had fevers?
Do you have night sweats?
Have you ever had pneumonia or tuberculosis?
Have you had a recent chest X-ray?
Have you had any bleeding or discharge from your breasts or felt any lumps there?
Gastrointestinal system
Are you troubled by indigestion?
Do you have heartburn?
Have you had any difficulty swallowing?
Have you had nausea or vomiting, or vomited blood?
Have you had pain or discomfort in your abdomen?
Have you had any abdominal bloating or distension?
Has your bowel habit changed recently?
How many bowel motions a week do you usually pass?
Have you lost control of your bowels or had accidents (faecal incontinence)?
Have you seen blood in your motions or vomited blood?
Have your bowel motions been black?
Have you lost weight recently?
Have your eyes or skin ever been yellow?
Have you ever had hepatitis, peptic ulceration, colitis, or bowel cancer?
Tell me about your diet recently.
Genitourinary system
Do you have difficulty or pain on passing urine?
Is your urine stream as good as it used to be?
Is there a delay before you start to pass urine? (Applies mostly to men.)
Is there dribbling at the end?
Do you have to get up at night to pass urine?
Are you passing larger or smaller amounts of urine?
Has the urine colour changed?
Have you seen blood in your urine?
Have you noticed any rashes or lumps on your genitals?
Have you ever had a sexually transmitted disease?

Have you ever had a urinary tract infection or kidney stone?

Are your periods regular?

Do you have excessive pain or bleeding with your periods?

Haematological system

Do you bruise easily?

Have you had fevers, or shivers and shakes (rigors)?

Do you have difficulty stopping a small cut from bleeding?

Have you noticed any lumps under your arms, or in your neck or groin?

Have you ever had blood clots in your legs or in the lungs?

Musculoskeletal system

Do you have painful or stiff joints?

Are your joints ever swollen?

Have you had a skin rash recently?

Do you have any back or neck pain?

Have your eyes been dry or red?

Have you ever had a dry mouth or mouth ulcers?

Have you been diagnosed as having rheumatoid arthritis or gout?

Do your fingers ever become painful and become white and blue in the cold?

Endocrine system

Have you noticed any swelling in your neck?

Do your hands tremble?

Do you prefer hot or cold weather?

Have you had a thyroid problem or diabetes?

Have you noticed increased sweating?

Have you been troubled by fatigue?

Have you noticed any change in your appearance, hair, skin or voice?

Have you been unusually thirsty lately?

Reproductive history (women)

Have you had any miscarriages?

Have you had high blood pressure or diabetes in pregnancy?

Neurological system and mental state

Do you get headaches?

Have you had memory problems or trouble concentrating?

Have you had fainting episodes, fits or blackouts?

Do you have trouble seeing or hearing?

Are you dizzy?

Have you had weakness, numbness or clumsiness in your arms or legs?

Have you ever had a stroke or head injury?

Have you had difficulty sleeping?

Do you feel sad or depressed, or have problems with your 'nerves'?

Have you ever been sexually or physically abused?

Examinations:

BP: **RESP RATE:**

PULSE: **TEMP:**

PRIMARY SURVEY:

C
A
J
C
O
L
D

CVS:

RESP:

ABDOMEN:

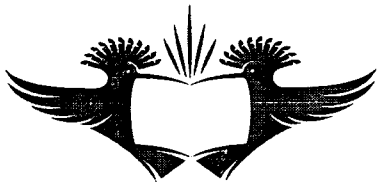
OTHER:

Investigations:

DATE;	BLEEDING TIME	PT	PTT

APPENDIX D

HOW TO TAKE YOUR MEDICATION



How to take your Medication

SCHEDULING STATUS:
Not scheduled:

COMPOSITION:
Each 25ml bottle contains:
Arnica montana 6C (not in placebo)
Preservative: 20% Ethanol

DOSAGE AND DIRECTIONS FOR USE:
Adults: 10 drops under the tongue twice a day at least half an hour before or after food

IDENTIFICATION:
A transparent liquid

PRESENTATION:
25mL amber glass bottle

STORAGE INSTRUCTIONS:
Store below 25°C.
Protect from light and moisture.
Keep away from strong odours including camphor.
KEEP OUT OF REACH OF CHILDREN.

There are no anticipated side effects for taking this medication. If you do however experience any unusual symptoms stop the medication and please contact the researcher or research supervisor .

Researcher: Thobela Nkunjana: 083 491 5687

Research supervisor: Dr B. Saunders: 011 559 6599 (084 424 6364)

APPENDIX E

HIGHER DEGREES COMMITTEE APPROVAL

UNIVERSITY OF JOHANNESBURG

FACULTY OF HEALTH SCIENCES
ACADEMIC ETHICS COMMITTEE

21 April 2008

Clearance Reference Number: 12/08

TO WHOM IT MAY CONCERN

TITLE OF RESEARCH PROJECT: "The effect of homoeopathic prepared arnica montana 6C on bleeding prothrombin and activated partial thommboplastin times in vivo"

RESEARCHER: Nkujana T

SUPERVISOR: Dr B Saunders

CO-SUPERVISOR: Dr U Hohl

The Committee for Academic Ethics of the Faculty of Health Sciences of the University of Johannesburg evaluated the research proposal and consent letters of the above research project and confirms that it complies with the approved Ethical Research Standards of University of Johannesburg.

Attached please find the recommended changes to improve the quality of your proposal.

Changes must re-submitted to the satisfactory of the supervisor/s.

Kind Regards

Ms M H SELOLO
FACULTY OFFICER: POSTGRADUATE PROGRAMMES